	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2250	lbp or (liposaccharide adj binding adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/04 10:16			0
2	BRS	L2	1750	septicemia	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/04 10:16			0
3	BRS	L3	0	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/04 10:16			0
4	BRS	L4	40	(lbp or (liposaccharide adj binding adj protein)) near (human or murine or rabbit or rat)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/04 10:19			0

=> d his

(FILE 'HOME' ENTERED AT 10:26:20 ON 04 APR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
10:27:11 ON 04 APR 2002
L1 4477 S LBP OR (LIPOSACCHARIDE BINDING PROTEIN)
L2 54235 S SEPTICEMIA
L3 12 S L1 (P) L2
L4 8 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5 1129 S L1 (P) (HUMAN OR MURINE)
L6 211530 S ENDOTOXIN OR LPS
L7 752 S L5 (P) L6
L8 291 S L7 (P) INHIBIT?
L9 79 DUPLICATE REMOVE L8 (212 DUPLICATES REMOVED)
L10 20 S L9 (P) INTERACT?
L11 18 S L10 NOT L4

=> log y

FILE 'HOME' ENTERED AT 10:26:20 ON 04 APR 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.42 TOTAL SESSION 0.42

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 10:27:11 ON 04 APR 2002

FILE 'CAPLUS' ENTERED AT 10:27:11 ON 04 APR 2002
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FILE 'AGRICOLA' ENTERED AT 10:27:11 ON 04 APR 2002

=> s lbp or (liposaccharide binding protein)
L1 4477 LBP OR (LIPOSACCHARIDE BINDING PROTEIN)

=> s septicemia
L2 54235 SEPTICEMIA

=> s l1 (p) l2
L3 12 L1 (P) L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 8 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> d l4 1-8 ibib abs

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:234499 CAPLUS
TITLE: Lactoferrin interacts with CD14s and inhibits the expression of endothelial adhesion molecules, induced by the CD14s-lipopolysaccharide complex
AUTHOR(S): Elass, E.; Baveye, S.; Fernig, D.; Blanquart, C.; Masson, M.; Mazurier, J.; Legrand, D.
CORPORATE SOURCE: Laboratoire de Chimie Biologique, Universite des Sciences et Technologies de Lille, Unite Mixte de Recherche 8576 du CNRS, Villeneuve d'Ascq, Fr.
SOURCE: Biochemistry and Cell Biology (2002), 80(1), 165
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lipopolysaccharides (LPS), either in the free form or complexed to CD14, a LPS receptor, are elicitors of the immune system. The endotoxin-chelating properties of lactoferrin (Lf) and its ability to compete with ***LBP*** for LPS binding explain in part the role of the protein in the modulation of inflammation. However, the optimal protection of animals against induced ***septicemia*** requires a 12-24 h pre-injection of Lf, that suggests that this protein may act by mechanisms addnl. to simple LPS scavenging. We hypothesized that interactions between Lf and sol. CD14 (sCD14) exist. In a first step, human sCD14 and human Lf (hLf) were used to det. the kinetic binding parameters of hLf to free sCD14 in an optical biosensor. The results demonstrated that hLf bound specifically and with a high affinity (Kd = 16 .+-. 7 nM) to sCD14. Affinity chromatog. studies showed that hLf interacted not only with free sCD14 but also, though with different binding properties, with sCD14 complexed to LPS or lipid

A-KDO-heptose. In a second step, we have investigated whether the capacity of hLf to interact with sCD14 could modulate the expression of E-selectin or ICAM-1 induced by the sCD14-LPS complex on human umbilical endothelial cells (HUVEC). Our expts. show that hLf significantly inhibited both E-selectin and ICAM-1 expressions at the surface of HUVEC. In conclusion, these observations suggest that the anti-inflammatory effects of hLf are due not only to the ability of the mol. to chelate LPS but also to its ability to interact with sCD14 and with the sCD14 complexed to LPS, thus modifying the activation of endothelial cells.

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:213536 CAPLUS
DOCUMENT NUMBER: 135:239863
TITLE: Pathophysiology of acute lung injury from an infection perspective
AUTHOR(S): Takahashi, Keiji; Suzuki, Satoshi; Tsuchihara, Katsuma; Tsuchihara, Chihara; Tobe, Takeyasu; Kasakura, Hisato; Tsuga, Hirohisa; Tsuga, Kazuhiro; Nambu, Yoshihiro; Okada, Tsuneto; Maebo, Yoshimasa; Takeda, Yuji; Ohya, Nobuo; Sakuma, Tsutomu
CORPORATE SOURCE: Dept. of Respiratory, Kanazawa Medical University, Japan
SOURCE: Kagaku Ryoho no Ryoiki (2001), 17(2), 361-371
CODEN: KRRYEI; ISSN: 0913-2384
PUBLISHER: Iyaku Janarusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 42 refs. on bacterial endotoxin recognition and its signal transduction by alveolar macrophages and host defense function of pulmonary surfactant proteins in acute lung injury caused by infection. Lipopolysaccharide (LPS) in causing acute lung injury, important role of LPS-binding protein (***LBP***) in LPS signal transduction by alveolar macrophages, induction of ***LBP*** gene expression by acute inflammatory-phase cytokines, prodn. of ***LBP*** by respiratory type II epithelial cells, .beta.-lactam antibiotics in influencing bacterial free endotoxin release and onsets of ***septicemia*** and acute respiratory distress syndrome (ARDS), and surfactant protein SP-A and SP-D in mediating organism adherence to host infectious defense mechanism are discussed.

L4 ANSWER 3 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000000383 MEDLINE
DOCUMENT NUMBER: 20000383 PubMed ID: 10532583
TITLE: Direct effects of endotoxin on the endothelium: barrier function and injury.
AUTHOR: Bannerman D D; Goldblum S E
CORPORATE SOURCE: Department of Pathology, Veterans Affairs Medical Center-Baltimore, University of Maryland School of Medicine, 21201, USA.
SOURCE: LABORATORY INVESTIGATION, (1999 Oct) 79 (10) 1181-99. Ref: 185
Journal code: KZ4; 0376617. ISSN: 0023-6837.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991103
AB LPS directly disrupts EC barrier function in vitro and in vivo. This barrier dysfunction has been reported to occur in EC derived from both the macro- and microvasculature of varying species, including humans. Unlike other EC responses, LPS-induced loss of endothelial barrier function is protein-synthesis independent. In fact, protein synthesis inhibition enhances the LPS effect. The lipid A moiety is responsible for LPS-induced activation of the non-CD14-bearing EC, and agents that bind to and neutralize this highly conserved portion of the LPS molecule can crossprotect against EC barrier dysfunction elicited by LPS derived from diverse species of Gram-negative bacteria. Although the presentation of

LPS to CD14-bearing cells such as macrophages and monocytes has been well characterized, far less is known about the interactions of LPS with the non-CD14-bearing EC. An EC receptor involved in LPS binding and cellular activation has yet to be identified. The presence of the accessory molecules, ***LBP*** and sCD14, are prerequisite to LPS-induced activation of EC at clinically relevant LPS concentrations. As with monocytes and macrophages, the CD14 dependence of LPS-induced endothelial barrier dysfunction can be overcome with high concentrations of LPS. In the absence of ***LBP*** and sCD14, a 200,000-fold increase in LPS concentration is required to elicit the same increments in EC monolayer permeability relative to when these accessory molecules are present. Within 30 minutes after LPS exposure, PTK activation is observed. PTK inhibition blocks LPS-induced EC actin depolymerization and endothelial barrier dysfunction which are seen only after a > or = 2-hour stimulus-to-response lag time. Furthermore this LPS-induced actin depolymerization is a prerequisite to opening up the paracellular pathway and loss of monolayer integrity. Interestingly LPS-induced increments in transendothelial 14C-BSA flux and EC detachment parallel caspase-mediated cleavage of ZA and FA proteins that participate in cell-cell and cell-matrix adhesion. The cleavage of the ZA components, beta- and gamma-catenin, does not affect their ability to bind the transmembrane protein, cadherin, or the actin-binding protein, alpha-catenin, suggesting that the linkage of the ZA to the actin cytoskeleton remains intact. LPS-induced cleavage of the FA protein, FAK, leads to dissociation of its catalytic domain from paxillin substrate and decreased paxillin phosphotyrosine content. Caspase inhibition protects against LPS-provoked apoptosis, cleavage of adherens junction proteins, paxillin dephosphorylation, cell-shape changes, and EC detachment. In contrast it fails to block LPS-induced increments in transendothelial 14C-BSA flux. PTK inhibition, which does protect against increased transendothelial 14C-BSA flux, does not block LPS-induced proteolytic cleavage events and only partially inhibits EC detachment. These findings suggest that the EC detachment and endothelial barrier dysfunction elicited by LPS are mediated through distinct pathways (Fig. 6). Much of the work to date has focused on LPS interactions with mCD14-bearing cells, such as monocytes and macrophages, which are central to the inflammatory response elicited by endotoxin. EC, which line the vasculature, are one of the first host tissue barriers to encounter circulating LPS. Because damage to the endothelium is known to contribute to the development of multiorgan failure, including ARDS, understanding LPS-induced EC dysfunction in the setting of Gram-negative ***septicemia*** has clear pathophysiologic implications. (ABSTRACT TRUNCATED)

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 1999:610347 CAPLUS
DOCUMENT NUMBER: 132:121434
TITLE: Purinergic receptor modulation of LPS-stimulated signaling events and nitric oxide release in RAW 264.7 macrophages
AUTHOR(S): Sommer, J. A.; Fisette, P. L.; Hu, Y.; Denlinger, L. C.; Guerra, A. N.; Bertics, P. J.; Proctor, R. A.
CORPORATE SOURCE: Department of Biomolecular Chemistry, University of Wisconsin Medical School, Madison, WI, 53706, USA
SOURCE: J. Endotoxin Res. (1999), 5(1/2), 70-74
CODEN: JENREB; ISSN: 0968-0519
PUBLISHER: Maney Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purinergic receptors of the P2 class are cell surface receptors which are sensitive to extracellular adenine nucleotides, such as ATP and ADP. This class of receptors is divided into the P2Y family of G protein-coupled receptors and the P2X family of ligand-gated ion channels. The P2X receptors, seven of which have been cloned, are thought to possess two transmembrane domains and function as multimeric complexes. Numerous studies have suggested a role for P2 receptors in activation of macrophages by Gram-neg. bacterial endotoxin (lipopolysaccharide; LPS). LPS is thought to exert its toxic effects, in large part, by inducing macrophages to release inflammatory mediators such as tumor necrosis factor .alpha. (TNF.alpha.), interleukin-1 (IL-1) and nitric oxide (NO). Although multiple signal transduction pathways are activated by LPS in macrophages, the proximal mechanisms by which LPS exerts these effects remain unclear. The current study examines the role of the P2X7/P2Z

purinergic receptor in LPS signaling events and in nitric oxide (NO) prodn. The results indicate that the P2X7 receptor is required for maximal LPS activation of the mitogen-activated protein (MAP) kinases extracellular signal-regulated kinase (ERK)1 and ERK2, for activation of nuclear factor (NF)-.kappa.B, as well as for upregulation of the inducible form of nitric oxide synthase (iNOS). These results are fortified by our recent observation that the C-terminus of the P2X7 receptor is homologous to conserved LPS binding domains of proteins crit. to host responses to Gram-neg. bacterial infection, such as LPS-binding protein (***LBP***) and bactericidal permeability-increasing protein (BPI). Taken together, these observations suggest that the P2X7 receptor plays a fundamental role in LPS signal transduction and activation of macrophages, and thus may represent a therapeutic target for Gram-neg. bacterial ***septicemia***
.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:823336 CAPLUS
DOCUMENT NUMBER: 123:222331
TITLE: Method for quantifying LBP in body fluids
INVENTOR(S): White, Mark Leslie; Carroll, Stephen Fitzhugh; Ma, Jeremy Kam-kuen
PATENT ASSIGNEE(S): Xoma Corp., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9520163	A1	19950727	WO 1995-US982	19950124
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5484705	A	19960116	US 1994-186811	19940124
CA 2181815	AA	19950727	CA 1995-2181815	19950124
AU 9517321	A1	19950808	AU 1995-17321	19950124
AU 701710	B2	19990204		
EP 741870	A1	19961113	EP 1995-909325	19950124
EP 741870	B1	19990714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1139485	A	19970101	CN 1995-191324	19950124
JP 09508465	T2	19970826	JP 1995-519741	19950124
AT 182216	E	19990715	AT 1995-909325	19950124
ES 2133738	T3	19990916	ES 1995-909325	19950124

PRIORITY APPLN. INFO.: US 1994-186811 A 19940124
WO 1995-US982 W 19950124

AB The present invention provides a method for quantifying the presence of extracellular LBP in body fluids including blood in a subject comprising conducting an LBP immunoassay on plasma obtained from said subject.

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:656263 CAPLUS
DOCUMENT NUMBER: 123:54030
TITLE: Lipopolysaccharide binding protein and CD14 modulate the synthesis of platelet-activating factor by human monocytes and mesangial and endothelial cells stimulated with lipopolysaccharide
AUTHOR(S): Camussi, Giovanni; Mariano, Rilippo; Biancone, Luigi; De Martino, Antonella; Bussolati, Benedetta; Montrucchio, Giuseppe; Tobias, Peter S.
CORPORATE SOURCE: Dep. Nephrol., Fac. Med. Surgery, Univ. Pavia, Varese, Italy
SOURCE: J. Immunol. (1995), 155(1), 316-24
CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The biosynthesis of platelet-activating factor (PAF) during Gram-neg. sepsis involves the interaction of LPS with the cells of the host. The authors have investigated the mol. mechanism that controls cell recognition and PAF biosynthetic response to LPS in human monocytes (MO), glomerular mesangial cells (MC), and HUVEC in culture. The synthesis of PAF by MO and MC involves two proteins, plasma LPS binding protein (LBP) and cell membrane CD14 (mCD14). As MO, MC were shown to express the mCD14 mol. by several mAbs. MO and mCD14-pos. MC were stimulated to synthesize PAF either by the 63D3 and IOM-2 mAbs or by the natural ligand LBP-LPS complex. Moreover, LeuM3, 28C5, and 18E12 mAbs that were themselves unable to stimulate the synthesis of PAF blocked PAF synthesis initiated by LBP-LPS complex. LBP was required for synthesis of PAF by MO. In MC, which synthesize PAF also after stimulation by LPS alone, the LBP was shown to speed and significantly enhance the synthesis of PAF. The sol. form of CD14 (sCD14), when added to MO stimulated with LBP-LPS complexes, inhibited the synthesis of PAF possibly by competing with mCD14. In contrast, sCD14 was shown to be required for LPS-induced synthesis of PAF by HUVEC, which did not express mCD14. Therefore, membrane receptors (mCD14) and plasma sol. proteins (LBP and sCD14) may enable different human cell types to synthesize PAF after LPS stimulation.

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:410556 CAPLUS
DOCUMENT NUMBER: 122:256429
TITLE: Bactericidal permeability-increasing protein or lipopolysaccharide-binding protein variants and fusion proteins for use in the treatment of endotoxemia and their manufacture
INVENTOR(S): Scott, Randal W.; Marra, Marian N.
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425476	A1	19941110	WO 1994-US4709	19940429
W: AU, CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9469429	A1	19941121	AU 1994-69429	19940429
JP 08511682	T2	19961210	JP 1994-524554	19940429
EP 760849	A1	19970312	EP 1994-917901	19940429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6265187	B1	20010724	US 1995-431517	19950501

PRIORITY APPLN. INFO.:
US 1993-56292 A 19930430
US 1993-165717 A 19931210
US 1989-310842 B2 19890214
US 1990-468696 A2 19900122
US 1990-567016 B2 19900813
US 1991-681551 A2 19910405
WO 1991-US5758 A2 19910813
US 1992-915720 A2 19920722
WO 1994-US4709 W 19940429

AB Variants of bactericidal permeability -increasing protein (BPI) or lipopolysaccharide-binding protein and fusion proteins of one or both proteins with an IgG are manufd. by expression of the corresponding gene. These proteins are intended for use in the treatment of endotoxemias and other endotoxin-related disorders. Construction of genes for these proteins and their expression in yeast is demonstrated. Analogs that retained their biol. functions were tested in a mouse endotoxin challenge system. The proteins were able to protect mice against challenge with LDs of endotoxin with survival rates of 80-100%.

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:577546 CAPLUS
DOCUMENT NUMBER: 121:177546
TITLE: Role of the lipopolysaccharide (LPS)-binding

protein/CD14 pathway in LPS induction of tissue factor expression in monocytic cells

AUTHOR(S): Steinemann, Susan; Ulevitch, Richard J.; Mackman, Nigel

CORPORATE SOURCE: Department Immunology, Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Arterioscler. Thromb. (1994), 14(7), 1202-9
CODEN: ARTTE5; ISSN: 1049-8834

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Endotoxic shock is assocd. with a coagulopathy, organ failure, and death. Tissue factor (TF) expression by monocytes exposed to bacterial endotoxin [lipopolysaccharide (LPS)] may mediate the coagulopathy and contribute to the high mortality of this disease. The authors examd. the role of the LPS-binding protein (LBP)/CD14 receptor pathway in the LPS induction of TF expression in human monocytic THP-1 cells and peripheral blood monocytes. In THP-1 cells, the threshold concn. of LPS required to induce TF activity in serum-free medium was reduced 20-fold by purified LBP, which also enhanced TF mRNA synthesis. Similarly, monocytes cultured in the presence of serum were induced to express TF antigen at LPS concns. 100 times lower than monocytes cultured in serum-free medium. An anti-LBP monoclonal antibody indicated that this effect was dependent on the presence of LBP in serum. LPS/LBP induction of TF activity and TF antigen expression in these monocytic cells were also inhibited by an anti-CD14 monoclonal antibody, indicating a requirement for the CD14 receptor. Thus, low levels of LPS (5-100 pg/mL) present during sepsis induce TF expression in monocytes via the LBP/CD14-dependent pathway.

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=> d his

     (FILE 'HOME' ENTERED AT 10:26:20 ON 04 APR 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:27:11 ON 04 APR 2002
L1          4477 S LBP OR (LIPOSACCHARIDE BINDING PROTEIN)
L2         54235 S SEPTICEMIA
L3            12 S L1 (P) L2
L4             8 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=>  s l1 (p) (human or murine)
   4 FILES SEARCHED...
L5         1129 L1 (P) (HUMAN OR MURINE)

=> s endotoxin or lps
L6       211530 ENDOTOXIN OR LPS

=> s l5 (p) l6
L7           752 L5 (P) L6

=> s l7 (p) inhibit?
L8           291 L7 (P) INHIBIT?

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L8
L9            79 DUPLICATE REMOVE L8 (212 DUPLICATES REMOVED)

=> s l9 (p) interact?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L58 (P) INTERACT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L60 (P) INTERACT?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L62 (P) INTERACT?'
L10           20 L9 (P) INTERACT?

=> d his

     (FILE 'HOME' ENTERED AT 10:26:20 ON 04 APR 2002)
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     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:27:11 ON 04 APR 2002
L1          4477 S LBP OR (LIPOSACCHARIDE BINDING PROTEIN)
L2         54235 S SEPTICEMIA
L3            12 S L1 (P) L2
L4             8 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5          1129 S L1 (P) (HUMAN OR MURINE)
L6        211530 S ENDOTOXIN OR LPS
L7           752 S L5 (P) L6
L8           291 S L7 (P) INHIBIT?
L9            79 DUPLICATE REMOVE L8 (212 DUPLICATES REMOVED)
L10           20 S L9 (P) INTERACT?

=> s l10 not l4
L11           18 L10 NOT L4

=> d l11 1-18 ibib abs

L11  ANSWER 1 OF 18     MEDLINE
ACCESSION NUMBER:    1999105555     MEDLINE
DOCUMENT NUMBER:     99105555   PubMed ID: 9890549
TITLE:               The three-dimensional structure of human
                     bactericidal/permeability-increasing protein: implications
                     for understanding protein-lipopolysaccharide interactions.
AUTHOR:              Beamer L J; Carroll S F; Eisenberg D
CORPORATE SOURCE:    Biochemistry Department, University of Missouri-Columbia
                     65211, USA.. beamerl@missouri.edu
SOURCE:              BIOCHEMICAL PHARMACOLOGY, (1999 Feb 1) 57 (3) 225-9.  Ref:
                     34
                     Journal code: 9Z4; 0101032. ISSN: 0006-2952.
PUB. COUNTRY:        ENGLAND: United Kingdom
                     Journal; Article; (JOURNAL ARTICLE)
                     General Review; (REVIEW)
                     (REVIEW, TUTORIAL)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199901
ENTRY DATE:          Entered STN: 19990209
                     Last Updated on STN: 19990209
                     Entered Medline: 19990126
AB   Gram-negative bacterial infections are often complicated by the
     inflammatory properties of lipopolysaccharides ( ***LPS*** ) on or
     released from the bacterial outer membrane. When present in the mammalian
     bloodstream, ***LPS*** can trigger a series of pathological changes,
     sometimes resulting in septic shock. Two related mammalian proteins,
     bactericidal/permeability-increasing protein (BPI) and
     lipopolysaccharide-binding protein ( ***LBP*** ), are known to affect
     the ***LPS*** -induced inflammatory response and are, therefore, of
     clinical interest. The recently determined three-dimensional structure of
     ***human*** BPI provides information on the overall protein fold, domain
     organization, and conserved regions of these two proteins. In addition,
     the discovery of two apolar lipid binding pockets in BPI indicates a
     possible site of ***interaction*** with ***LPS*** . The BPI
     structure is a powerful tool for the design of site-directed mutants,
     peptide mimetics/ ***inhibitors*** , and BPI/ ***LBP*** chimeras.
     These studies should help further define the functions of BPI and
     ***LBP*** , and their mechanism of ***interaction*** with ***LPS***
     .

L11  ANSWER 2 OF 18     MEDLINE
ACCESSION NUMBER:    1998227852     MEDLINE
DOCUMENT NUMBER:     98227852   PubMed ID: 9568897
TITLE:               The BPI/LBP family of proteins: a structural analysis of
                     conserved regions.
AUTHOR:              Beamer L J; Carroll S F; Eisenberg D
CORPORATE SOURCE:    Biochemistry Department, University of Missouri-Columbia,
                     65211, USA.
SOURCE:              PROTEIN SCIENCE, (1998 Apr) 7 (4) 906-14.
                     Journal code: BNW; 9211750. ISSN: 0961-8368.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
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FILE SEGMENT: Priority Journals
OTHER SOURCE: SWISSPROT-P17[redacted]; SWISSPROT-P17453; SWISSPROT-[redacted]454; SWISSPROT-P18428; SWISSPROT-Q28739; SWISSPROT-Q61805; SWISSPROT-Q63313
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980604

AB Two related mammalian proteins, bactericidal/permeability-increasing protein (BPI) and lipopolysaccharide-binding protein (***LBP***), share high-affinity binding to lipopolysaccharide (***LPS***), a glycolipid found in the outer membrane of gram-negative bacteria. The recently determined crystal structure of ***human*** BPI permits a structure/function analysis, presented here, of the conserved regions of these two proteins sequences. In the seven known sequences of BPI and ***LBP*** , 102 residues are completely conserved and may be classified in terms of location, side-chain chemistry, and ***interactions*** with other residues. We find that the most highly conserved regions lie at the interfaces between the tertiary structural elements that help create two apolar lipid-binding pockets. Most of the conserved polar and charged residues appear to be involved in inter-residue ***interactions*** such as H-bonding. However, in both BPI and ***LBP*** a subset of conserved residues with positive charge (lysines 42, 48, 92, 95, and 99 of BPI) have no apparent structural role. These residues cluster at the tip of the NH2-terminal domain, and several coincide with residues known to affect ***LPS*** binding; thus, it seems likely that these residues make electrostatic ***interactions*** with negatively charged groups of ***LPS*** . Overall differences in charge and electrostatic potential between BPI and ***LBP*** suggest that BPI's bactericidal activity is related to the high positive charge of its NH2-terminal domain. A model of ***human*** ***LBP*** derived from the BPI structure provides a rational basis for future experiments, such as site-directed mutagenesis and ***inhibitor*** design.

L11 ANSWER 3 OF 18 MEDLINE
ACCESSION NUMBER: 1998114345 MEDLINE
DOCUMENT NUMBER: 98114345 PubMed ID: 9453600
TITLE: Lactoferrin inhibits the endotoxin interaction with CD14 by competition with the lipopolysaccharide-binding protein.
AUTHOR: Elass-Rochard E; Legrand D; Salmon V; Roseanu A; Trif M; Tobias P S; Mazurier J; Spik G
CORPORATE SOURCE: Unite Mixte de Recherche de CNRS no. 111, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq, France.
SOURCE: INFECTION AND IMMUNITY, (1998 Feb) 66 (2) 486-91.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980224
Last Updated on STN: 19980224
Entered Medline: 19980212

AB ***Human*** lactoferrin (hLf), a glycoprotein released from neutrophil granules during inflammation, and the lipopolysaccharide (***LPS***)-binding protein (***LBP***), an acute-phase serum protein, are known to bind to the lipid A of ***LPS*** . The ***LPS*** -binding sites are located in the N-terminal regions of both proteins, at amino acid residues 28 to 34 of hLf and 91 to 108 of ***LBP*** . Both of these proteins modulate ***endotoxin*** activities, but they possess biologically antagonistic properties. In this study, we have investigated the competition between hLf and recombinant ***human*** ***LBP*** (rhLBP) for the binding of Escherichia coli 055:B5 ***LPS*** to the differentiated monocytic THP-1 cell line. Our studies revealed that hLf prevented the rhLBP-mediated binding of ***LPS*** to the CD14 receptor on cells. Maximal ***inhibition*** of ***LPS*** -cell ***interactions*** by hLf was raised when both hLf and rhLBP were simultaneously added to ***LPS*** or when hLf and ***LPS*** were mixed with cells 30 min prior to the incubation with rhLBP. However, when hLf was added 30 min after the ***interaction*** of rhLBP with ***LPS*** , the binding of the rhLPS- ***LBP*** complex to CD14 could

not be reversed. These observations indicate that hLf competes with rhLBP for the ***LPS*** binding and therefore interferes with the ***interaction*** of ***LPS*** with CD14. Furthermore, experiments involving competitive binding of the rhLBP- ***LPS*** complex to cells with two recombinant mutated hLfs show that in addition to residues 28 to 34, another basic cluster which contains residues 1 to 5 of hLf competes for the binding to ***LPS*** . Basic sequences homologous to residues 28 to 34 of hLf were evidenced on ***LPS*** -binding proteins such as ***LBP*** , bactericidal/permeability-increasing protein, and Limulus anti- ***LPS*** factor.

L11 ANSWER 4 OF 18 MEDLINE
ACCESSION NUMBER: 96399085 MEDLINE
DOCUMENT NUMBER: 96399085 PubMed ID: 8805656
TITLE: Mycobacterial lipoarabinomannan recognition requires a receptor that shares components of the endotoxin signaling system.
AUTHOR: Savedra R Jr; Delude R L; Ingalls R R; Fenton M J; Golenbock D T
CORPORATE SOURCE: The Maxwell Finland Laboratory for Infectious Diseases, Department of Medicine, Boston City Hospital, MA 02118, USA.
CONTRACT NUMBER: AI94-16 (NIAID)
GM47127 (NIGMS)
HL07501 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Sep 15) 157 (6) 2549-54.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961212

AB Phagocytic leukocytes respond to a variety of bacterial products including Gram-negative bacterial ***LPS*** and mycobacterial lipoarabinomannan (LAM). Anti-CD14 mAbs have been shown to block ***LPS*** and LAM activation of myeloid cells, suggesting that CD14 is required for cellular recognition of both ligands. Activation of undifferentiated promonomyelocytic THP-1 cells with LAM or ***LPS*** under serum-free conditions was enhanced in the presence of recombinant soluble CD14 (rsCD14). ***LPS*** binding protein (***LBP***), which is present in normal serum, further enhanced the sensitivity of undifferentiated THP-1 cells to both ligands even in the absence of rsCD14. Although CD14-transfected Chinese hamster ovary and ***human*** HT1080 fibrosarcoma cell lines can be activated by ***LPS*** , neither cell line was activated by LAM. Furthermore, U373 astrocytoma cells, which respond to ***LPS*** using sCD14 and ***LBP*** , failed to be activated by LAM in the presence of rsCD14 and rLBP. We then tested the effects of lipid IVA and Rhodobacter sphaeroides lipid A, compounds that function as ***endotoxin*** ***inhibitors*** in ***human*** cells by ***interacting*** with a molecule thought to be a CD14-dependent ***LPS*** signal transducer. Both lipid IVA and R. sphaeroides lipid A ***inhibited*** the effects of ***LPS*** and LAM in THP-1 cells. Thus, the ***LPS*** and LAM receptors share CD14, ***LBP*** , and a putative ***endotoxin*** antagonist-***inhibitable*** signal transducing component. However, the LAM signaling system appears to require an additional receptor component whose expression is restricted to cells of hemopoietic origin.

L11 ANSWER 5 OF 18 MEDLINE
ACCESSION NUMBER: 96384683 MEDLINE
DOCUMENT NUMBER: 96384683 PubMed ID: 8792567
TITLE: Purification of lipopolysaccharide-binding protein from bovine serum.
AUTHOR: Bochsler P N; Yang Z; Murphy C L; Carroll R C
CORPORATE SOURCE: Department of Pathology, College of Veterinary Medicine, University of Tennessee, Knoxville 37901, USA.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1996 Jun 1) 51 (3-4) 303-14.
Journal code: XCB; 8002006. ISSN: 0165-2427.

PUB. COUNTRY: Netherlands
Journal; Arti ; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970203

AB Lipopolysaccharide-binding protein (***LBP***) plays a central role in presentation of bacterial-derived lipopolysaccharide (***LPS*** ; ***endotoxin***) to leukocytes such as macrophages and neutrophils. ***Interaction*** of ***LBP*** with ***LPS*** is significant because ***LBP*** - ***LPS*** complexes promote activation of leukocytes and the immune system, which results in enhanced secretion of a spectrum of proinflammatory cytokines. An improved, simplified method was used to purify bovine ***LBP*** from serum. Methodology consisted of ion-exchange chromatography using Bio-Rex 70 resin, followed by gel-filtration chromatography (Sephacryl S-200 resin) of a selected ion-exchange fraction (0.22-0.50 M NaCl). Densitometric scans on silver-stained polyacrylamide gels of chromatographically-derived proteins indicated up to 88.7% purity of the resultant 64kD protein (bovine ***LBP***) in the cleanest fractions. The isoelectric point of bovine ***LBP*** was determined to be 6.8. Identity of the protein was substantiated by western-blot analysis, and by N-terminus amino acid sequence analysis with favorable comparison to published sequence data from rabbit, ***human*** , and ***murine*** ***LBP*** Identity was corroborated by use of purified bovine ***LBP*** in bioassays which demonstrated enhanced tissue factor expression of ***LPS*** (1 ng ml(-1)-stimulated bovine alveolar macrophages. Tissue factor expression was ***inhibitable*** in these assays using anti-CD14 monoclonal antibodies, which is also consistent with ***LBP*** -mediated activation of cells. When bovine ***LBP*** was heated at 56 degrees C for 30 min, the biological activity was reduced by 50% in the macrophage-based bioassays. Biological activity of bovine ***LBP*** was completely destroyed by heating at 62 degrees C for 30 min, which compared favorably with data resulting from use of fetal bovine serum.

L11 ANSWER 6 OF 18 MEDLINE
ACCESSION NUMBER: 96218127 MEDLINE
DOCUMENT NUMBER: 96218127 PubMed ID: 8647810
TITLE: Neutralization and transfer of lipopolysaccharide by phospholipid transfer protein.
AUTHOR: Hailman E; Albers J J; Wolfbauer G; Tu A Y; Wright S D
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021, USA.
CONTRACT NUMBER: AI 30556 (NIAID)
HL 30086 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 24) 271 (21) 12172-8.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960805
Last Updated on STN: 19960805
Entered Medline: 19960722

AB Phospholipid transfer protein (PLTP) and lipopolysaccharide-binding protein (LPB) are lipid transfer proteins found in ***human*** plasma. PLTP shares 24% sequence similarity with ***LBP*** . PLTP mediates the transfer and exchange of phospholipids between lipoprotein particles, whereas ***LBP*** transfers bacterial lipopolysaccharide (***LPS***) either to lipoprotein particles or to CD14, a soluble and cell-surface receptor for ***LPS*** . We asked whether PLTP could ***interact*** with ***LPS*** and mediate the transfer of ***LPS*** to lipoproteins or to CD14. PLTP was able to bind and neutralize ***LPS*** : incubation of ***LPS*** with purified recombinant PLTP (rPLTP) resulted in the ***inhibition*** of the ability of ***LPS*** to stimulate adhesive responses of neutrophils, and addition of rPLTP to blood ***inhibited*** cytokine production in response to ***LPS*** . Transfer of ***LPS*** by rPLTP was examined using fluorescence

dequenching experiments and native gel electrophoresis. The results suggested that rPLTP was able to mediate the exchange of ***LPS*** between micelles and the transfer of ***LPS*** to reconstituted HDL particles, but it did not transfer ***LPS*** to CD14. Consonant with these findings, rPLTP did not mediate CD14-dependent adhesive responses of neutrophils to ***LPS*** . These results suggest that while PLTP and ***LBP*** both bind and transfer ***LPS*** , PLTP is unable to transfer ***LPS*** to CD14 and thus does not mediate responses of cells to ***LPS*** .

L11 ANSWER 7 OF 18 MEDLINE
ACCESSION NUMBER: 96158377 MEDLINE
DOCUMENT NUMBER: 96158377 PubMed ID: 8588345
TITLE: Characterisation of bovine lipopolysaccharide binding protein and the in vivo acute phase response to Pasteurella haemolytica Type A.
AUTHOR: Horadagoda N U; Eckersall P D; Andrew L; Gallay P; Heumann D; Gibbs H A
CORPORATE SOURCE: Department of Veterinary Medicine, Glasgow University Veterinary School, Bearsden, UK.
SOURCE: VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (1995 Nov) 49 (1-2) 61-74.
Journal code: XCB; 8002006. ISSN: 0165-2427.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960404
Last Updated on STN: 19960404
Entered Medline: 19960327
AB Lipopolysaccharide binding protein (***LBP***) is a liver-derived acute phase protein which is implicated in modulating the host responses to lipopolysaccharide (***LPS***) from Gram-negative bacteria. ***LBP*** ***interacts*** with circulatory ***LPS*** to form complexes which bind to the CD14 receptor or cells of the monocytic lineage and neutrophils resulting in their activation. This causes the release of mediators and cytokines which are responsible for initiating the acute phase response. ***LBP*** -like activity has now been identified in bovine serum and in this study ***LBP*** has been purified from acute phase bovine serum using ion exchange chromatography. On sodium dodecyl sulphate polyacrylamide electrophoresis, bovine ***LBP*** demonstrated a single band with a molecular mass of 58 kDa. Bovine ***LBP*** enhanced the binding of ***LPS*** to ***human*** monocytes while enzymatic removal of the CD14 receptor abrogated this ***interaction*** . Furthermore, bovine ***LBP*** increased the sensitivity of monocytes to ***LPS*** by at least 100-fold. Depletion of ***LBP*** by means of antibodies to bovine ***LBP*** ***inhibited*** the serum mediated ***LPS*** binding to monocytes. Antibodies to rabbit ***LBP*** or recombinant ***human*** ***LBP*** did not cross-react with bovine ***LBP*** . Studies on the kinetics of ***LBP*** activity in calves during the acute phase response demonstrated a four-fold increase in the serum concentration 36 h after a single intratracheal inoculation of Pasteurella haemolytica A1. The findings of this study indicate that cattle possess a ***LPS*** detection mechanism comparable to that described in man and experimental animals in which ***LBP*** forms complexes in serum with circulatory ***LPS*** enhancing the signal to the immune system to mount a host response. The isolation of ***LBP*** will allow further investigations into ***LBP*** -mediated responses to ***LPS*** in cattle.

L11 ANSWER 8 OF 18 MEDLINE
ACCESSION NUMBER: 95325604 MEDLINE
DOCUMENT NUMBER: 95325604 PubMed ID: 7541418
TITLE: Lipopolysaccharide binding protein and CD14 modulate the synthesis of platelet-activating factor by human monocytes and mesangial and endothelial cells stimulated with lipopolysaccharide.
AUTHOR: Camussi G; Mariano F; Biancone L; De Martino A; Bussolati B; Montrucchio G; Tobias P S
CORPORATE SOURCE: Department of Nephrology, Faculty of Medicine and Surgery,

University of Pavia, Varese, Italy.
CONTRACT NUMBER: AI32021 (NIAID)
HL23584 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1995 Jul 1) 155 (1) 316-24.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950822
Last Updated on STN: 19960129
Entered Medline: 19950807

AB The biosynthesis of platelet-activating factor (PAF) during Gram-negative involves the ***interaction*** of ***LPS*** with the cells of the host. We have investigated the molecular mechanism that controls cell recognition and PAF biosynthetic response to ***LPS*** in ***human*** monocytes (MO), glomerular mesangial cells (MC), and HUVEC in culture. The synthesis of PAF by MO and MC involves two proteins, plasma ***LPS*** binding protein (***LBP***) and cell membrane CD14 (mCD14). As MO, MC were shown to express the mCD14 molecule by several mAbs. MO and mCD14-positive MC were stimulated to synthesize PAF either by the 63D3 and IOM-2 mAbs or by the natural ligand ***LBP*** - ***LPS*** complex. Moreover, LeuM3, 28C5, and 18E12 mAbs that were themselves unable to stimulate the synthesis of PAF blocked PAF synthesis initiated by ***LBP*** - ***LPS*** complex. ***LBP*** was required for synthesis of PAF by MO. In MC, which synthesize PAF also after stimulation by ***LPS*** alone, the ***LBP*** was shown to speed and significantly enhance the synthesis of PAF. The soluble form of CD14 (sCD14), when added to MO stimulated with ***LBP*** - ***LPS*** complexes, ***inhibited*** the synthesis of PAF possibly by competing with mCD14. In contrast, sCD14 was shown to be required for ***LPS*** -induced synthesis of PAF by HUVEC, which did not express mCD14. Therefore, membrane receptors (mCD14) and plasma soluble proteins (***LBP*** and sCD14) may enable different ***human*** cell types to synthesize PAF after ***LPS*** stimulation.

L11 ANSWER 9 OF 18 MEDLINE
ACCESSION NUMBER: 95247783 MEDLINE
DOCUMENT NUMBER: 95247783 PubMed ID: 7537270
TITLE: Enzymatically deacylated lipopolysaccharide (LPS) can antagonize LPS at multiple sites in the LPS recognition pathway.
AUTHOR: Kitchens R L; Munford R S
CORPORATE SOURCE: Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235, USA.
CONTRACT NUMBER: AI18188 (NIAID)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Apr 28) 270 (17) 9904-10.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950608
Last Updated on STN: 19960129
Entered Medline: 19950601

AB Like other tetraacyl partial structures of lipopolysaccharide (***LPS***) and lipid A, ***LPS*** that has been partially deacylated by acyloxyacyl hydrolase can ***inhibit*** ***LPS*** -induced responses in ***human*** cells. To identify the site(s) of ***inhibition*** in the ***LPS*** recognition pathway, we analyzed the apparent binding affinities and ***interactions*** of 3H-labeled enzymatically deacylated ***LPS*** (dLPS) and [3H] ***LPS*** with CD14, the ***LPS*** receptor, on THP-1 cells. Using (i) incubation conditions that prevented ligand internalization and (ii) defined concentrations of ***LPS*** binding protein (***LBP***), which facilitates ***LPS*** and dLPS binding to CD14, we found that dLPS can antagonize ***LPS*** in at least three ways. 1) When the concentration of ***LBP*** in the medium was suboptimal for promoting ***LPS*** -CD14 binding, low concentrations of dLPS were able to compete with

LPS for binding CD14, suggesting competition between ***LPS*** and dLPS for engaging ***[redacted]*** . 2) When ***LBP*** was present in excess, dLPS could compete with ***LPS*** for binding CD14, but only at dLPS concentrations that were at or above its KD for binding CD14 (100 ng/ml). 3) In contrast, substoichiometric concentrations of dLPS (1 ng/ml) ***inhibited*** ***LPS*** -induced (3 ng/ml) interleukin-8 release without blocking ***LPS*** binding to CD14. Functional antagonism was possible without competition for cell-surface binding because both ***LPS*** -induced interleukin-8 release and dLPS ***inhibition*** occurred at concentrations that were far below their respective CD14 binding KD values. In addition to its expected ability to compete with ***LPS*** for binding ***LBP*** and CD14, dLPS thus potently antagonizes ***LPS*** at an undiscovered site that is distal to ***LPS*** -CD14 binding in the ***LPS*** recognition pathway.

L11 ANSWER 10 OF 18 MEDLINE
ACCESSION NUMBER: 95088501 MEDLINE
DOCUMENT NUMBER: 95088501 PubMed ID: 7996053
TITLE: Identification and characterization of a bovine lipopolysaccharide-binding protein.
AUTHOR: Khemlani L S; Yang Z; Bochsler P N
CORPORATE SOURCE: Department of Pathology, University of Tennessee College of Veterinary Medicine, Knoxville.
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1994 Dec) 56 (6) 784-91. Journal code: IWY; 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950126
Last Updated on STN: 19950126
Entered Medline: 19950119

AB Endogenous regulatory mechanisms exist in mammals that enable a rapid response to lipopolysaccharide (***LPS*** , ***endotoxin***) stemming from gram-negative bacterial infections. Serum proteins and cell surface receptors exist that bind ***LPS*** , and this ***interaction*** may either aid in nonpathogenic removal of ***LPS*** from the body or potentiate the effects of ***LPS*** . We have used a photoreactive, thiol-cleavable, radiolabeled derivative of E. coli 0111:B4 ***LPS*** [***LPS*** -(p-azidosalicylamido)-1,3'-dithiopropionamide; 125I-ASD- ***LPS***], to identify the presence of ***LPS*** -binding proteins (***LBPs***) in bovine serum. Ion exchange chromatography was used to fractionate bovine serum, and eluted protein was subsequently photoaffinity labeled using 125I-ASD- ***LPS*** . ***LBPs*** were identified by autoradiography of sodium dodecyl sulfate-polyacrylamide gels. Several ***LBPs*** including three with apparent molecular masses of 65, 60, and 50 kDa were variably present within the chromatography pools. A 22-residue NH2-terminal amino acid sequence of the 60-kDa protein showed 77% homology with ***human*** ***LBP*** and 68% with rabbit ***LBP*** within this region. Further purification utilizing high-performance liquid chromatography yielded a protein fraction that contained the 60-kDa protein and was distinctly more active than whole bovine serum in ***LPS*** -dependent macrophage activation assays (up to 1600-fold on a weight/volume basis). The ***LPS*** -mediated macrophage activation in concert with chromatographically purified serum protein in tissue factor assays was ***inhibitable*** using anti-CD14 monoclonal antibodies. The results indicate that an ***LPS*** -binding protein exists in samples of pooled bovine serum and that this protein has features in common with ***human*** and rabbit ***LBP*** .

L11 ANSWER 11 OF 18 MEDLINE
ACCESSION NUMBER: 94194123 MEDLINE
DOCUMENT NUMBER: 94194123 PubMed ID: 7511654
TITLE: An amino-terminal fragment of human lipopolysaccharide-binding protein retains lipid A binding but not CD14-stimulatory activity.
AUTHOR: Theofan G; Horwitz A H; Williams R E; Liu P S; Chan I; Birr C; Carroll S F; Meszaros K; Parent J B; Kasler H; +
CORPORATE SOURCE: XOMA Corporation, Santa Monica, CA 90404.
SOURCE: JOURNAL OF IMMUNOLOGY, (1994 Apr 1) 152 (7) 3623-9.

Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-M35533
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940511
Last Updated on STN: 19960129
Entered Medline: 19940429

AB ***LPS*** -binding protein (***LBP***) mediates the pro-inflammatory effects of bacterial ***LPS*** by enhancing ***LPS*** -induced cytokine production by monocytic cells. ***LBP*** binds specifically to ***LPS*** to generate a complex that ***interacts*** with the CD14 receptor on the surface of responsive cells. To identify the biologically active regions of the protein responsible for mediating these activities, we cloned and expressed ***human*** rLBP (456 amino acids) as well as a truncated form encoding amino acids 1-197 (rLBP25). Both forms of ***LBP*** bound to ***LPS*** with the same affinity, and similarly ***inhibited*** ***LPS*** activity in the Limulus amebocyte lysate assay. These results demonstrate that the ***LPS*** -binding domain of ***LBP*** resides entirely within the N-terminal 197 amino acids of the protein. rLBP and rLBP25 were compared for their ability to mediate CD14-dependent ***LPS*** effects on cells. rLBP was effective in mediating uptake of ***LPS*** and stimulation of TNF production by ***human*** monocytic THP-1 cells, whereas rLBP25 had no significant activity in these assays. Similarly, rLBP was able to mediate ***LPS*** -induced TNF production by ***human*** PBMC whereas rLBP25 was essentially inactive. These results suggest that the structural features of ***LBP*** required for mediating ***LPS*** effects via CD14 are probably located in the C-terminal region of the protein. Thus, the ***LPS*** -binding activity of ***LBP*** can be separated from the CD14-stimulatory activity, suggesting these activities are mediated by structural elements residing in different regions of the protein.

L11 ANSWER 12 OF 18 MEDLINE
ACCESSION NUMBER: 94179192 MEDLINE
DOCUMENT NUMBER: 94179192 PubMed ID: 7510680
TITLE: Lipopolysaccharide (LPS) binding protein, truncated at Ile-197, binds LPS but does not transfer LPS to CD14.
AUTHOR: Han J; Mathison J C; Ulevitch R J; Tobias P S
CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, California 92037.
CONTRACT NUMBER: AI15136 (NIAID)
AI32021 (NIAID)
GM37696 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Mar 18) 269 (11) 8172-5.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940428
Last Updated on STN: 19960129
Entered Medline: 19940418

AB Lipopolysaccharide (***LPS***) binding protein (***LBP***), a 58-60 kDa glycoprotein, binds to the lipid A region of ***LPS*** . The resulting ***LPS*** - ***LBP*** complex is recognized by both the membrane-bound (mCD14) and soluble forms of CD14 (sCD14), thereby enhancing the ability of ***LPS*** to activate myeloid, endothelial, and epithelial cells. To begin to characterize the structure-function relationships within ***LBP*** , we have created and expressed a truncated form of ***human*** ***LBP*** (herein called NH- ***LBP***) comprising amino acid residues 1-197 of the parent molecule. Experiments were done to characterize the ability of NH- ***LBP*** to bind ***LPS*** and to promote ***LPS*** binding to CD14. We found that NH- ***LBP*** efficiently binds ***LPS*** but does not transfer the ***LPS*** to either mCD14 or sCD14. Additionally, NH- ***LBP*** ***inhibited*** ***LPS*** binding to ***LBP*** ,

inhibited the ***LBP*** -promoted binding of ***LPS*** to CD14, and ***inhibited*** the ***LBP*** -dependent activation of rabbit peritoneal exudate macrophages. The apparent dissociation constant for ***LPS*** -NH- ***LBP*** complexes is less than 1 x 10(-8) M which compares well with the dissociation constant for ***LPS*** - ***LBP*** complexes of approximately 1 x 10(-9) M. We conclude from these studies that the ***LPS*** binding site of ***LBP*** resides in the amino-terminal half of ***LBP*** and that the CD14 ***interaction*** site resides in the carboxyl-terminal half of ***LBP*** . These data suggest that appropriately modified fragments of ***LBP*** might provide novel reagents with high ***LPS*** binding affinity that could be useful in ***inhibiting*** ***LPS*** -dependent cellular activation in vivo.

L11 ANSWER 13 OF 18 MEDLINE
ACCESSION NUMBER: 94043342 MEDLINE
DOCUMENT NUMBER: 94043342 PubMed ID: 7693705
TITLE: Analysis of lipopolysaccharide binding by CD14.
AUTHOR: Kirkland T N; Finley F; Leturcq D; Moriarty A; Lee J D; Ulevitch R J; Tobias P S
CORPORATE SOURCE: Department of Pathology and Medicine, University of California, San Diego.
CONTRACT NUMBER: AI15136 (NIAID)
GM28485 (NIGMS)
GM37696 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Nov 25) 268 (33) 24818-23.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19960129
Entered Medline: 19931220

AB The cell surface protein CD14 binds bacterial lipopolysaccharide (***LPS***) in the presence of the serum protein, ***LPS*** -binding protein (***LBP***). This ***interaction*** is important for ***LPS*** -induced activation of mammalian myeloid cells. We performed quantitative studies of 3H-labeled ***LPS*** binding to ***human*** CD14 expressed on Chinese hamster ovary cells and on a ***human*** macrophage cell line (THP-1). At the concentrations studied (20-100 nM) ***LPS*** binding required the expression of CD14 and could be ***inhibited*** by a subset of anti-CD14 monoclonal antibodies. ***LBP*** was required for ***LPS*** binding to CD14. The binding occurred within 10 min and was relatively unaffected by temperature over the range of 4-37 degrees C. Quantitative binding assays were performed at 10 degrees C, or at 37 degrees C, using Chinese hamster ovary cells depleted of ATP. In both cases, 75-90% of the ***LPS*** could be released by treatment with phosphatidylinositol-specific phospholipase C, suggesting that it remains associated with the glycosyl phosphatidylinositol-anchored CD14. The apparent dissociation constant of recombinant ***human*** CD14 expressed on Chinese hamster ovary cells for ***LPS*** at 10 degrees C was 2.74 (+/- 0.99) x 10(-8) M; the apparent dissociation constant of CD14 expressed on THP-1 cells at 10 degrees C was 4.89 (+/- 1.42) x 10(-8) M. In both cell lines, at saturating ***LPS*** concentrations, the molar ratio of ***LPS*** bound per surface CD14 was approximately 20:1. At 37 degrees C the apparent dissociation constant of recombinant ***human*** CD14 for ***LPS*** at 37 degrees C was 2.7 (+/- 1.2) x 10(-8) M, and the molar ratio of ***LPS*** bound per surface CD14 was approximately 8:1. Although the difference in molar ratio of ***LPS*** bound per surface CD14 at the two temperatures is difficult to interpret, it is clear that at both temperatures the molar ratio is not 1:1. The basis of this phenomenon is unclear, but may involve the repeated leucine-rich motifs, which are found within CD14.

L11 ANSWER 14 OF 18 MEDLINE
ACCESSION NUMBER: 93203621 MEDLINE
DOCUMENT NUMBER: 93203621 PubMed ID: 7681085
TITLE: Cross-linking of lipopolysaccharide (LPS) to CD14 on THP-1

cells mediated by LPS-binding protein.
AUTHOR: Tobias P S; [redacted]au K; Kline L; Lee J D; Kato K[redacted]artin T P; Ulevitch R J
CORPORATE SOURCE: Scripps Research Institute, La Jolla, CA 92037.
CONTRACT NUMBER: AI15136 (NIAID)
AI25563 (NIAID)
GM28485 (NIGMS)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Apr 1) 150 (7) 3011-21.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 19960129
Entered Medline: 19930420

AB Recent work has established that bacterial ***endotoxin*** (***LPS***) binds to the plasma protein ***LPS*** -binding protein (***LBP***) forming high affinity complexes (***LPS*** - ***LBP***), that ***LBP*** is an opsonin for ***LPS*** -bearing particles, and that ***LPS*** - ***LBP*** complexes are potent agonists for monocytic cells (MO). mAb to the MO plasma membrane protein, CD14, ***inhibit*** ***LBP*** -dependent binding of ***LPS*** to MO, and ***LPS*** - ***LBP*** -dependent stimulation of cytokine release from MO. These data suggest that CD14 functions as a membrane receptor for ***LPS*** but do not demonstrate a direct association of ***LPS*** with CD14. Calcitriol was used to induce a high level of CD14 expression in the ***human*** monocyte-like cell line THP-1, resulting in enhanced responses of these cells to ***LPS*** - ***LBP*** complexes manifested by enhanced binding of ***LPS*** and a decrease in the amount of ***LPS*** needed to induce IL-8 release. An Re595 ***LPS*** derivative containing a radioiodinated, photoreactive, phenyl azide (125I-ASD- ***LPS***) was used in cross-linking experiments to identify membrane proteins in calcitriol-treated THP-1 cells that ***interact*** with ***LPS*** . 125I-ASD- ***LPS*** was added to calcitriol-induced THP-1 cells in the presence or absence of ***LBP*** , the mixture photolyzed, and the resultant radioiodinated proteins analyzed by SDS-PAGE and autoradiography. We observed strong cross-linking of 125I-ASD- ***LPS*** to a 55-kDa membrane protein when ***LBP*** was present, but failed to observe radiolabeling of any other proteins with apparent molecular masses distinct from CD14. The cross-linked product was identified as CD14 by immunoprecipitation with anti- ***human*** CD14 mAb. Studies with ***human*** CD14 expressing transfectants of the ***murine*** B cell line 70Z/3 also revealed ***LBP*** -dependent cross-linking of 125I-ASD- ***LPS*** to CD14. These data document binding of ***LPS*** to a specific membrane protein that serves as an ***LPS*** receptor.

L11 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 92268491 MEDLINE
DOCUMENT NUMBER: 92268491 PubMed ID: 1375247
TITLE: Control of lipopolysaccharide (LPS) binding and LPS-induced tumor necrosis factor secretion in human peripheral blood monocytes.
AUTHOR: Heumann D; Gallay P; Barras C; Zaech P; Ulevitch R J; Tobias P S; Glauser M P; Baumgartner J D
CORPORATE SOURCE: Department of Internal Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.
CONTRACT NUMBER: AI15136 (NIAID)
AI25536 (NIAID)
GM28485 (NIGMS)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1992 Jun 1) 148 (11) 3505-12.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920710

Last Updated on STN: 19960129
Entered Medli[redacted] 19920625

AB We used flow cytometry to determine how ***LPS*** -binding protein (***LBP***) effects the binding of fluorescein-labeled ***LPS*** to ***human*** monocytes via receptor-dependent mechanisms. The addition of ***human*** , rabbit, mouse, or FCS strikingly increased the binding of ***LPS*** to monocytes compared with controls incubated in serum-free medium. This binding was totally prevented by preincubation of monocytes with MY4, an anti-CD14 mAb, or by enzymatic removal of CD14 from monocytes. Depletion of ***LBP*** from rabbit serum with anti- ***LBP*** antibodies also produced a similar suppression. Solutions of albumin did not support the enhanced binding observed in serum but the addition of purified rabbit ***LBP*** to albumin solutions resulted in binding similar to that observed in serum-containing medium. When type-specific anti- ***LPS*** mAb was added to ***human*** serum, ***LPS*** binding to monocytes occurred but was only partly ***inhibited*** by anti-CD14 mAb, suggesting that receptors other than CD14 (presumably Fc or complement receptors) were involved. Serum increased by 100- to 1000-fold the sensitivity of monocytes to the triggering by ***LPS*** resulting in TNF secretion. TNF secretion was ***inhibited*** by anti-CD14 mAb up to 100 ng/ml of ***LPS*** and by anti- ***LPS*** mAb up to 1 to 10 ng/ml. The ***inhibition*** of TNF secretion by anti- ***LPS*** mAb appeared to be the result of directing ***LPS*** to monocyte receptors other than CD14. In contrast, in medium containing normal as well as acute serum and in the absence of anti- ***LPS*** antibodies, the binding of ***LPS*** to monocytes and the triggering of TNF secretion appeared to be mediated mainly by ***interactions*** between CD14 and ***LBP*** - ***LPS*** complexes.

L11 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:637301 CAPLUS
TITLE: Rhizobia produce lipopolysaccharides with unusual lipid A structures and the ability to prevent enteric LPS-induced cytokine production
AUTHOR(S): Carlson, Russell W.; Jeyaretnam, B. S.; Vandenplas, M. L.; McNeill, B. W.; Barton, M. H.; Norton, N.; Moore, J. N.
CORPORATE SOURCE: Complex Carbohydrate Research Center, University of Georgia, Athens, GA, 30602, USA
SOURCE: Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United States, August 26-30, 2001 (2001), CARB-036. American Chemical Society: Washington, D. C.
CODEN: 69BUZP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB ***LPS*** is a component of gram-neg. bacteria and is a potent inflammatory substance inducing the prodn. of cytokines and other inflammatory substances. The inflammatory nature of the ***LPS*** lies largely in the lipid portion of this mol. known as the lipid A. The lipid A from enteric bacteria is commonly a bis-phosphorylated fatty acylated glucosamine disaccharide. The structural features of the lipid A responsible for its inflammatory properties include the presence of the phosphate groups, and the type, location and no. of fatty acyl substituents. The activity of the ***LPS*** occurs via ***interaction*** of the ***LPS*** with cluster differentiation antigen, CD14, and with Toll-like receptor 4; and is facilitated with the plasma protein, ***LPS*** -binding protein (***LBP***). Various labs. have worked to identify both natural and synthetic lipid A analogs which interfere with the ***interaction*** of ***LPS*** with inflammatory cells; i.e are lipid-A antagonists. Some of these analogs have antagonistic activity on ***human*** cells but are agonistic in other species or have limited shelf life (e.g. the ***LPS*** /lipid A from Rhodobacter spharoides). Certain species of the nitrogen-fixing soil bacteria, rhizobia, have very novel lipid A structures. These structures generally lack acyloxyacyl residues, lack phosphate, and can have a very long C28 fatty acyl residue. Some structures contain lipid A in which reducing-end glucosamine residue is converted to 2-aminogluconate, and the 4'-phosphate group is replaced by a galacturonosyl residue. A single Rhizobium strain can contain a no. of different lipid A mols. due to heterogeneity in the fatty acyl substitution pattern, and due to the fact

that the 2-aminoglucononic acid residue can be present in both the free-acid and lactone forms. The LPSs from several Rhizobium strains do not stimulate either ***human*** or equine cells to produce tumor necrosis factor (TNF). Furthermore, rhizobial LPSs can ***inhibit*** the ability of enteric LPSs to induce TNF. Part of the reason for this effect is the ability of the rhizobial LPSs to interfere with the binding of enteric LPSs to ***LBP*** .

L11 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:510551 CAPLUS
DOCUMENT NUMBER: 129:274546
TITLE: Identification of the lipopolysaccharide (LPS) binding site of LPS binding protein (LBP) by site-directed mutagenesis: evidence for a similar LPS recognition mechanism in different LPS binding proteins
AUTHOR(S): Lamping, N.; Hoess, A.; Yu, B.; Park, T. C.; Wright, S. D.; Kirschning, C. J.; Pfeil, D.; Herrmann, F.; Schumann, R. R.
CORPORATE SOURCE: Labor fuer Molekulare Sepsisforschung, Max-Delbrueck-Centrum fuer, Humboldt-Universitaet zu Berlin, Berlin, Germany
SOURCE: Immune Consequences Trauma, Shock Sepsis, Int. Congr., 4th (1997), 15-19. Editor(s): Faist, Eugen. Monduzzi Editore: Bologna, Italy.
CODEN: 66MUAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB ***Human*** ***LPS*** (***endotoxin***) Binding Protein (***LBP***) is capable of binding ***LPS*** of Gram-neg. bacteria and transporting it to the ***LPS*** receptor CD14, a process of potential importance for inflammatory reactions and the septic shock syndrome. Here we report on the identification of a region of ***human*** ***LBP*** which is involved in ***LBP*** - ***LPS*** ***interaction*** employing short synthetic ***LBP*** -peptides covering the entire ***LBP*** amino acid sequence. Peptides according to the region of amino acids 81 to 110 exhibited ***inhibitory*** activity on ***LPS*** - ***LBP*** ***interaction*** . ***LBP*** point mutations within this region of ***LBP*** were investigated by different functional assays. A double mutant Glu 94 / Glu 95 failed to display any ***LPS*** binding and cell stimulatory activity. Furthermore, exchange of this region of ***LBP*** by the postulated ***LPS*** binding regions of bactericidal/permeability increasing protein and Limulus anti- ***LPS*** factor (LALF) was able to retain ***LBP*** activity.

L11 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:469517 CAPLUS
DOCUMENT NUMBER: 129:243778
TITLE: Bacterial cell envelopes (ghosts) and LPS but not bacterial S-layers induce synthesis of immune-mediators in mouse macrophages involving CD14
AUTHOR(S): Haslberger, A. G.; Mader, H. J.; Schmalnauer, M.; Kohl, G.; Szostak, M. P.; Messner, P.; Sleytr, U. B.; Wanner, G.; Furst-Ladani, S.; Lubitz, W.
CORPORATE SOURCE: Institute of Microbiology and Genetics, Biocenter, University of Vienna, Vienna, A-1030, Austria
SOURCE: J. Endotoxin Res. (1997), 4(6), 431-441
CODEN: JENREB; ISSN: 0968-0519
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of inflammatory mediators in ***human*** macrophages/monocytes seen after stimulation with lipopolysaccharide (***LPS***) involves the binding of CD14 to ***LPS*** complexed to lipopolysaccharide binding protein (***LBP***). The binding mechanisms of different ***LPS*** domains to ***LBP*** and CD14, as well as the ***interaction*** of the entire bacterial cell wall and its components with CD14 and ***LBP*** , are poorly understood. The authors, therefore, studied the effects of anti-mouse CD14 antibodies on the synthesis of TNF.alpha. and PGE2 in RAW 264.7 mouse macrophages stimulated by bacterial cell envelopes (ghosts) of Escherichia coli O26:B6 and Salmonella typhimurium C5, ***LPS*** , lipid A, and cryst.

bacterial cell surface layer (S-layer) prepns. Ghosts and S-layers, with distinct activities on the immune-system, are presently under investigation for their use as vaccines. Whereas ***LPS*** and E. coli ghosts exhibited a strong endotoxic activity in the Limulus amoebocyte lysate assay, the endotoxic activity of S-layer prepns. was several orders of magnitude lower. ***LPS*** , ghosts, and bacterial S-layers all induced TNF.alpha. and PGE2 synthesis as well as the accumulation of TNF.alpha. mRNA. Pre-incubation with anti-mouse CD14 antibodies resulted in a dose-dependent ***inhibition*** of TNF.alpha. and PGE2 synthesis after stimulation by ***LPS*** , lipid A (30-50%) and ghosts (40-70%). The bacterial S-layer-induced mediator synthesis remained unchanged following the addn. of anti-mouse CD14 antibodies. Reproducible differences could be obsd. for the ***inhibition*** of TNF.alpha. induced by ***LPS*** of different species by anti-CD14. Adding fetal calf serum (FCS) strongly enhanced the release of cell mediators stimulated by low doses of ***LPS*** and bacterial ghosts. These effects of the FCS may be due to the presence of ***LBP*** in the FCS. The results show that CD14 is highly relevant for the activation of mouse macrophages by bacterial cells, ***LPS*** , and lipid A. Specially defined bacterial cell wall constituents such as bacterial S-layers might act through other activation pathways.

=> d his

(FILE 'HOME' ENTERED AT 10:26:20 ON 04 APR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:27:11 ON 04 APR 2002

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L1          4477 S LBP OR (LIPOSACCHARIDE BINDING PROTEIN)
L2         54235 S SEPTICEMIA
L3            12 S L1 (P) L2
L4             8 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5          1129 S L1 (P) (HUMAN OR MURINE)
L6        211530 S ENDOTOXIN OR LPS
L7           752 S L5 (P) L6
L8           291 S L7 (P) INHIBIT?
L9            79 DUPLICATE REMOVE L8 (212 DUPLICATES REMOVED)
L10           20 S L9 (P) INTERACT?
L11           18 S L10 NOT L4
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=> log y

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